

73

SEQUENCE LISTING

<110> Ng, Gordon
O'Neill, Gary P.

<120> USE OF GABAPENTIN IN ASSAYS TO IDENTIFY
GABAB RECEPTOR AGONISTS, INVERSE AGONISTS, ANTAGONISTS, AND
ALLOSTERIC MODULATORS OF AGONISTS

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<140> 09/980,437

<141> 2002-11-30

<150> PCT/CA00/00638

<151> 2000-05-30

<150> 60/137,025

<151> 1999-06-01

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Trp	Lys	Lys	Ile	Ala	Thr	Ile	Gln	Gln	Thr	Thr	Glu	Val	Phe	Thr	Ser
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Thr	Leu	Asp	Asp	Leu	Glu	Glu	Arg	Val	Lys	Glu	Ala	Gly	Ile	Glu	Ile
				325					330					335	
Thr	Phe	Arg	Gln	Ser	Phe	Phe	Ser	Asp	Pro	Ala	Val	Pro	Val	Lys	Asn
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Glu	Ala	Arg	Lys	Val	Phe	Cys	Glu	Val	Tyr	Lys	Glu	Arg	Leu	Phe	Gly
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Lys	Lys	Tyr	Val	Trp	Phe	Leu	Ile	Gly	Trp	Tyr	Ala	Asp	Asn	Trp	Phe
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Lys	Thr	Tyr	Asp	Pro	Ser	Ile	Asn	Cys	Thr	Val	Glu	Glu	Met	Thr	Glu
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Ala	Val	Glu	Gly	His	Ile	Thr	Thr	Glu	Ile	Val	Met	Leu	Asn	Pro	Ala
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Glu	Ala	Pro	Leu	Ala	Tyr	Asp	Ala	Ile	Trp	Ala	Leu	Ala	Leu	Ala	Leu
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Phe	Asn	Tyr	Asn	Asn	Gln	Thr	Thr	Thr	Asp	Gln	Ile	Tyr	Arg	Ala	Met
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Trp	Ser	Lys	Thr	Asp	Lys	Trp	Ile	Gly	Gly	Ser	Pro	Pro	Ala	Asp	Gln
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Val	Leu	Thr	Leu	Ala	Ile	Trp	Gln	Ile	Val	Asp	Pro	Leu	His	Arg	Thr
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Ile	Leu	Pro	Gln	Leu	Glu	His	Cys	Ser	Ser	Lys	Lys	Met	Asn	Thr	Trp
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Phe	Ala	Phe	Ala	Ser	Leu	Ala	Ile	Val	Phe	Ser	Ser	Tyr	Ile	Thr	Leu
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Val	Val	Leu	Phe	Val	Pro	Lys	Met	Arg	Arg	Leu	Ile	Thr	Arg	Gly	Glu
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Leu	Glu	Lys	Ile	Ala	Glu	Lys	Glu	Glu	Arg	Val	Ser	Glu	Leu	Arg	
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Thr	Pro	Pro	Asp	Pro	Ser	Gly	Gly	Leu	Pro	Arg	Gly	Pro	Ser	Glu	Pro
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<211> 962

<212> PRT

<213> Homo Sapiens

<400> 22

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Cys	Leu	Ala	Asn	Gly	Ser	Trp	Thr	Asp	Met	Asp	Thr	Pro	Ser	Arg	Cys
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Val	Arg	Ile	Cys	Ser	Lys	Ser	Tyr	Leu	Thr	Leu	Glu	Asn	Gly	Lys	Val
			100					105					110		
Phe	Leu	Thr	Gly	Gly	Asp	Leu	Pro	Ala	Leu	Asp	Gly	Ala	Arg	Ala	Asp

Phe	Arg 130	Cys	Asp	Pro	Asp	Phe 135	His	Leu	Val	Gly	Ser 140	Ser	Arg	Ser	Ile
Cys 145	Ser	Gln	Gly	Gln	Trp 150	Ser	Thr	Pro	Lys	Pro 155	His	Cys	Gln	Val	Asn 160
Arg	Thr	Pro	His	Ser 165	Glu	Arg	Arg	Ala	Val 170	Tyr	Ile	Gly	Ala	Leu 175	Phe
Pro	Met	Ser	Gly 180	Gly	Trp	Pro	Gly	Gly 185	Gln	Ala	Cys	Gln	Pro	Ala	Val
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Tyr	Glu 210	Leu	Lys	Leu	Ile	His 215	His	Asp	Ser	Lys	Cys 220	Asp	Pro	Gly	Gln
Ala 225	Thr	Lys	Tyr	Leu	Tyr 230	Glu	Leu	Leu	Tyr	Asn 235	Asp	Pro	Ile	Lys	Ile 240
Ile	Leu	Met	Pro	Gly 245	Cys	Ser	Ser	Val	Ser 250	Thr	Leu	Val	Ala	Glu 255	Ala
Ala	Arg	Met	Trp 260	Asn	Leu	Ile	Val	Leu 265	Ser	Tyr	Gly	Ser	Ser 270	Ser	Pro
Ala	Leu	Ser 275	Asn	Arg	Gln	Arg	Phe 280	Pro	Thr	Phe	Phe	Arg 285	Thr	His	Pro
Ser	Ala 290	Thr	Leu	His	Asn	Pro 295	Thr	Arg	Val	Lys	Leu 300	Phe	Glu	Lys	Trp
Gly 305	Trp	Lys	Lys	Ile	Ala 310	Thr	Ile	Gln	Gln	Thr 315	Thr	Glu	Val	Phe	Thr 320
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Ile	Thr	Phe 340	Arg	Gln	Ser	Phe	Phe 345	Ser	Asp	Pro	Ala	Val	Pro 350	Val	Lys
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Gly 385	Lys	Lys	Tyr	Val	Trp 390	Phe	Leu	Ile	Gly	Trp 395	Tyr	Ala	Asp	Asn	Trp 400
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Ala	Asn	Thr 435	Arg	Ser	Ile	Ser	Asn 440	Met	Thr	Ser	Gln	Glu 445	Phe	Val	Glu
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Met	Asn 515	Ser	Ser	Ser	Phe	Glu	Gly 520	Val	Ser	Gly	His	Val 525	Val	Phe	Asp
Ala	Ser 530	Gly	Ser	Arg	Met	Ala 535	Trp	Thr	Leu	Ile	Glu 540	Gln	Leu	Gln	Gly
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Ser	Trp	Ser	Lys	Thr 565	Asp	Lys	Trp	Ile	Gly 570	Gly	Ser	Pro	Pro	Ala	Asp
Gln	Thr	Leu 580	Val	Ile	Lys	Thr	Phe 585	Arg	Phe	Leu	Ser	Gln	Lys 590	Leu	Phe
Ile	Ser	Val 595	Ser	Val	Leu	Ser	Ser 600	Leu	Gly	Ile	Val	Leu 605	Ala	Val	Val
Cys	Leu	Ser	Phe	Asn	Ile	Tyr	Asn	Ser	His	Val	Arg	Tyr	Ile	Gln	Asn

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625	630	635
Leu Ala Ala Val Phe	Pro Leu Gly Leu Asp	Gly Tyr His Ile Gly Arg
645	650	655
Asn Gln Phe Pro Phe	Val Cys Gln Ala Arg	Leu Trp Leu Leu Gly Leu
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Gly Phe Ser Leu Gly	Tyr Gly Ser Met Phe	Thr Lys Ile Trp Trp Val
675	680	685
His Thr Val Phe Thr	Lys Lys Glu Glu Lys	Lys Glu Trp Arg Lys Thr
690	695	700
Leu Glu Pro Trp Lys	Leu Tyr Ala Thr Val	Gly Leu Leu Val Gly Met
705	710	715
Asp Val Leu Thr Leu	Ala Ile Trp Gln Ile	Val Asp Pro Leu His Arg
725	730	735
Thr Ile Glu Thr Phe	Ala Lys Glu Glu Pro	Lys Glu Asp Ile Asp Val
740	745	750
Ser Ile Leu Pro Gln	Leu Glu His Cys Ser	Ser Arg Lys Met Asn Thr
755	760	765
Trp Leu Gly Ile Phe	Tyr Gly Tyr Lys Gly	Leu Leu Leu Leu Gly
770	775	780
Ile Phe Leu Ala Tyr	Glu Thr Lys Ser Val	Ser Thr Glu Lys Ile Asn
785	790	795
Asp His Arg Ala Val	Gly Met Ala Ile Tyr	Asn Val Ala Val Leu Cys
805	810	815
Leu Ile Thr Ala Pro	Val Thr Met Ile Leu	Ser Ser Gln Gln Asp Ala
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Ala Phe Ala Phe Ala	Ser Leu Ala Ile Val	Phe Ser Ser Tyr Ile Thr
835	840	845
Leu Val Val Leu Phe	Val Pro Lys Met Ile	Arg Arg Leu Ile Thr Arg
850	855	860
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Thr Asn Asn Asn Glu	Glu Glu Lys Ser Arg	Leu Leu Glu Lys Glu Asn
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Arg Glu Leu Glu Lys	Ile Ile Ala Glu Lys	Glu Glu Arg Val Ser Glu
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Leu Arg His Gln Leu	Gln Ser Arg Gln Gln	Leu Arg Ser Arg Arg His
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Pro Pro Thr Pro Pro	Glu Pro Ser Gly Gly	Leu Pro Arg Gly Pro Pro
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<211> 16
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 <213> HArtificial Sequence

<220>
 <223> Homo Sapiens

<400> 25
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<210> 26
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Homo Sapiens

<400> 26
 Asp Tyr Lys Asp Asp Asp Asp Lys
 1 5

<210> 27
 <211> 753
 <212> PRT
 <213> Caenorhabditis Elegans

<400> 27
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 Ala Ser Ala Glu Pro Val Thr Leu His Ile Gly Gly Thr Phe Pro Met
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 35 40 45
 Val Glu Met Ala Leu Lys Asp Val Asn Ser Arg Leu Asp Ile Leu Pro
 50 55 60
 Gly Tyr Val Leu Asn Met Thr Asn His Asn Ser Gln Cys Gln Pro Gly
 65 70 75 80
 Leu Ala Met Gln Gln Leu Tyr Asp Phe Leu Tyr Lys Pro Pro Thr Lys
 85 90 95
 Leu Met Leu Leu Thr Gly Cys Ser Pro Val Thr Thr Val Ile Ala Glu
 100 105 110
 Ala Ala Pro Val Trp Lys Leu Val Val Leu Ser Tyr Gly Gly Ser Ser
 115 120 125
 Pro Ala Leu Ser Asn Arg Asn Arg Phe Pro Thr Leu Phe Arg Thr His
 130 135 140
 Pro Ser Ala Asn Met Gln Asn Pro Thr Arg Ile His Ile Met Glu Lys
 145 150 155 160
 Phe Lys Trp Lys Arg Phe Thr Ile Leu Met Ser Val Glu Glu Val Phe
 165 170 175
 Val Thr Thr Ala Lys Asp Leu Glu Val Ser Glu Arg Lys Lys Gly Ile
 180 185 190
 Lys Val Asp Arg Gln Ser Phe Tyr Gly Asp Pro Thr Asp Ala Met Lys
 195 200 205
 Thr Leu Gln Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Val
 210 215 220
 Thr Glu Ala Arg Lys Val Leu Cys Gln Ala Tyr His His Gly Leu Tyr
 225 230 235 240
 Gly Arg Arg Tyr Val Trp Phe Phe Ile Gly Trp Tyr Ala Asp Thr Trp
 245 250 255
 Tyr Ile Pro Pro Pro Glu Glu His Leu Asn Cys Thr Ala Glu Gln Met

Thr	Glu	Ala	Ala	Glu	Tyr	His	Phe	Thr	Thr	Glu	Ser	Val	Met	Leu	Ser
		275					280					285			
Arg	Asp	Asn	Ile	Pro	Ala	Ile	Ser	Glu	Met	Thr	Gly	Met	Gln	Phe	Gln
	290					295					300				
Gln	Arg	Leu	Thr	Gln	Tyr	Phe	Gln	Lys	Asp	Thr	Ala	Asn	Val	Gly	Gly
305					310					315					320
Phe	Pro	Glu	Ala	Pro	Leu	Ala	Tyr	Asp	Ala	Val	Trp	Ala	Leu	Ala	Leu
				325					330					335	
Ala	Phe	Asn	Cys	Thr	Arg	Asn	Asn	Leu	Pro	Ser	His	Ile	Arg	Leu	Glu
			340					345					350		
Asn	Phe	Thr	Tyr	Asp	Asn	Lys	Val	Ile	Ala	Asp	Thr	Leu	Phe	Gln	Cys
		355					360					365			
Val	Lys	Asn	Thr	Ser	Phe	Arg	Gly	Val	Ser	Gly	Lys	Val	Met	Phe	Ser
	370					375					380				
Asp	Ser	Gly	Asp	Arg	Ile	Ala	Arg	Thr	Gln	Ile	Glu	Gln	Met	Gln	Gly
385					390					395					400
Gly	Lys	Tyr	Lys	Ile	Met	Gly	Tyr	Tyr	Asp	Thr	Thr	Ser	Gly	Asp	Leu
				405					410					415	
Glu	Trp	Tyr	Asn	Lys	Glu	Gln	Trp	Leu	Asn	Gly	Lys	Gly	Pro	Pro	Pro
			420					425					430		
Asp	Ser	Thr	Val	Ile	Lys	Thr	Phe	Asn	Ser	Tyr	Ser	Asp	Phe	Leu	Ile
		435					440					445			
Phe	Ser	Ser	Thr	Ile	Leu	Gln	Tyr	Phe	Ser	Gln	Phe	Leu	Ala	Leu	Leu
	450					455					460				
His	Val	Ser	Ser	Phe	Thr	Phe	Leu	His	Lys	Asn	Ile	Ile	Phe	Gln	Ser
465					470					475					480
Gln	Pro	Glu	Cys	Asn	Asn	Ile	Leu	Leu	Ile	Gly	Cys	Ser	Leu	Cys	Leu
				485					490					495	
Phe	Ser	Leu	Phe	Leu	Ile	Gly	Leu	Pro	Ser	Asp	Asp	Ile	Ser	Ile	Ser
			500					505					510		
Glu	Ser	Leu	Phe	Pro	Leu	Leu	Cys	His	Ala	Arg	Val	Thr	Ile	Leu	Leu
		515					520					525			
Phe	Gly	Phe	Thr	Phe	Ala	Tyr	Gly	Ser	Met	Phe	Ala	Lys	Val	Trp	Ile
	530					535					540				
Val	His	Arg	Met	Gly	Ala	Thr	Glu	Asn	Gln	Gln	Leu	Ala	Ser	Arg	Gln
545					550					555					560
Pro	Ile	Ser	Ser	Ser	Lys	Phe	Tyr	Val	Ile	Val	Ala	Ala	Leu	Thr	Ala
				565					570					575	
Val	Asp	Val	Phe	Val	Cys	Phe	Val	Trp	Val	Leu	Ile	Asp	Pro	Leu	His
			580					585					590		
Leu	Thr	Glu	Gln	Lys	Phe	Pro	Leu	Phe	Ala	Asp	Ser	Glu	Glu	Asp	Glu
		595					600					605			
Met	Ile	Met	Pro	Val	Leu	Gln	Gln	Cys	Gln	Ser	Asn	Gln	Gln	Glu	Val
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<210> 28
 <211> 659
 <212> PRT
 <213> Caenorhabditis Elegans

<400> 28
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 Thr Ala Leu Ser His Val His Ser Arg Ser Cys Ile Leu Gln Gly Tyr
 35 40 45
 Arg Leu Glu Met Ile Val Lys Asp Thr His Cys Lys Thr Ser Gln Gly
 50 55 60
 Met Lys Ala Leu Phe Asp Leu Ile Ala Ser Arg Pro Arg Pro Val Ala
 65 70 75 80
 Ile Leu Gly Gly Gln Cys Thr Glu Val Asn Glu Pro Ile Ala Met Ala
 85 90 95
 Leu Lys Tyr Trp Gln Ile Val Gln Leu Ser Tyr Ala Glu Thr His Ala
 100 105 110
 Met Asn Gly Gln Leu Gln Leu Phe Thr Thr Phe Phe Arg Val Val Pro
 115 120 125
 Gly Ser Arg Asn Thr Asn Met Ala Lys Cys Lys Phe Val Asn His Phe
 130 135 140
 Gly Trp Lys Arg Val Gly Thr Val Lys Gln Asn Asp Gln Pro Arg Tyr
 145 150 155 160
 Ala Leu Val Arg Asp Val Arg Ile Ile Leu Val Asp Val Asp Glu Glu
 165 170 175
 Met Ala Ala Thr Val Leu Cys Ala Gly Tyr His Arg Gly Met Tyr Gly
 180 185 190
 Asp Asn Tyr Val Trp Ile Leu Pro Gly Tyr His Ser Asp Arg Trp Leu
 195 200 205
 Asn Gln Thr His Asp Asn Cys Thr Val Glu Glu Met Arg Glu Ala Ala
 210 215 220
 Lys Asn His Phe Ser Val Glu Phe Ala Leu Thr Arg Arg Asp Val Asp
 225 230 235 240
 Thr Lys Ile Val Gly Asn Thr Val Ser Pro Tyr Val Thr Leu Asn Leu
 245 250 255
 Phe Gln Arg Ala Gly Asp Val Trp Asn Glu Ile Thr Gln Leu Asp Pro
 260 265 270
 Asn Asn Thr Trp Arg Gly Tyr Leu Tyr Asp Gly Leu Trp Thr Leu Ala
 275 280 285
 Ile Ala Leu Ser His Ser Met Gly Asp Asn Ala Glu Phe Ser His His
 290 295 300
 Lys Met Met Glu Ala Ile Asp Asn Ser Ser Phe Gln Gly Leu Thr Gly
 305 310 315 320
 Lys Val Lys Phe Ala Asn Asn Glu Arg Leu Gly Leu Val Asp Ile Lys
 325 330 335
 Gln Trp Ser Asp Gly Gln Tyr Val Pro Phe Ala Val Tyr Asp Gly Ala
 340 345 350
 Asp Asp Glu Phe Lys Ile Ile Asp Ser Thr Thr Lys Gly Trp Ser Pro
 355 360 365
 Pro Leu Asp Ser Thr Ile Thr Glu Arg Arg Arg Glu His Ile Ser Ser
 370 375 380
 Ile Leu Phe Leu Ala Met Ser Leu Leu Ala Leu Ile Gly Ile Phe Leu
 385 390 395 400
 Ala Leu Ile Phe Leu Leu Ile Asn Phe Arg Tyr Arg Asn His Arg Phe
 405 410 415
 Ile Lys Met Ser Pro Asn Leu Asn Asn Ile Ile Ile Ala Gly Ser
 420 425 430

Ile	Cys	Thr	Phe	Ala	Ser	Val	Ile	Met	Leu	Gly	Leu	Asp	Thr	Arg	Ile
		435					440					445			
Val	Ser	Pro	Asp	Val	Phe	Val	Trp	Leu	Cys	Tyr	Thr	Lys	Thr	Trp	Thr
	450					455					460				
Leu	Cys	Ile	Gly	Phe	Thr	Leu	Ser	Phe	Gly	Ala	Met	Phe	Ser	Lys	Thr
465					470					475					480
Trp	Arg	Val	His	Ser	Ile	Phe	Thr	Asn	Ile	Arg	Met	Asp	Arg	Lys	Ala
			485					490						495	
Ile	Lys	Asp	Ser	Lys	Leu	Phe	Ile	Ile	Leu	Gly	Ile	Leu	Leu	Phe	Ile
			500					505					510		
Asp	Ile	Cys	Val	Leu	Val	Thr	Trp	Ala	Phe	Val	Ser	Pro	Phe	Ser	Tyr
	515						520					525			
Thr	Val	Glu	Gln	Phe	Lys	Phe	Leu	Ile	Phe	Ser	Ala	Arg	Arg	Asn	Ile
	530					535					540				
Val	Ile	Ile	Pro	Glu	Val	Glu	Lys	Cys	Asn	Ser	Ser	His	Ser	Gly	Val
545					550					555					560
Phe	Gln	Ala	Val	Leu	Tyr	Ala	Val	Lys	Gly	Val	Leu	Met	Ile	Leu	Gly
			565						570					575	
Cys	Phe	Leu	Ala	Trp	Glu	Thr	Arg	His	Val	Asn	Val	Pro	Ala	Leu	Asn
			580					585					590		
Asp	Ser	Lys	Tyr	Ile	Gly	Thr	Ser	Val	Tyr	Cys	Cys	Val	Val	Met	Ser
	595						600					605			
Val	Leu	Gly	Leu	Ser	Thr	Ser	Val	Ile	Leu	Gln	Glu	Arg	Val	Asn	Glu
	610					615					620				
Met	Phe	Ser	Leu	Ala	Ser	Phe	Phe	Val	Ile	Phe	Ser	Thr	Thr	Leu	Thr
625					630					635					640
Leu	Cys	Leu	Val	Phe	Val	Pro	Lys	Val	Arg	Phe	Leu	Glu	Leu	Cys	Cys
				645					650					655	
Ile	Gly	Ser													